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EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,562	VENEMA, FOKKE	
	Examiner	Art Unit	
	AMANDA SHAW	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-41 and 43-55* is/are pending in the application.

4a) Of the above claim(s) *20-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-41 and 43-55* is/are rejected.

7)☒ Claim(s) *44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/3/2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/9/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group II (claims 39-55) in the reply filed on March 25, 2008 is acknowledged. The traversal is on the ground(s) that the Applicant disagrees with the conclusion in the Restriction Requirement that the special technical feature linking groups I and II of the present invention are molecular beacon probes containing 2'-O-methyl nucleotides. The Applicant submits that the special technical feature linking groups I and II are probes containing one or more nucleotides or nucleotide analogues having an affinity increasing modification **and** one or more unmodified nucleotides. Since Tsourkas describes molecular beacons consisting of continuous stretches of 2'-O-methyl substituted nucleotides with no unmodified nucleotides in the stem or the loop of the molecular beacons, this reference does not teach or suggest the probes of the present invention. Therefore Applicants believe that groups I and II of the present invention form a single general inventive concept that indeed defines a contribution over the prior art and should be searched and examined together. This is not found persuasive because even if the special technical feature is probes containing one or more nucleotides or nucleotide analogues having an affinity increasing modification **and** one or more unmodified nucleotides, the prior art of Becker (US 2003/0105320 Filed 8/2002) also teaches probes containing one or more nucleotides or nucleotide analogues having an affinity increasing modification **and** one or more unmodified nucleotides (See example 8) and could be used to break unity.

The requirement is still deemed proper and is therefore made FINAL.

Claims 20-41 and 43-55 are currently pending. Claims 20-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 39-41 and 43-55 have been examined herein.

Specification

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below:

Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims even if the sequence is also embedded in the text of the description or claims of the patent application. In the instant case the description contains sequences that are set forth in the Sequence Listing that are not identified by SEQ ID Nos (Tables 1-3).

Claim Objections

3. Claim 44 is objected to because it depends from the method of claim 42 and claim 42 has been cancelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-41 and 43-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39-41 and 43-52 are indefinite over the recitation of the phrase "unmodified nucleic acid". This phrase is indefinite because it is not clearly defined in the claims or the specification. The claims do not state any structural properties of the unmodified probe and do not define what the unmodified probe is being compared to.

Claims 40-41 and 43-52 are indefinite over the recitation of the phrase "said probe allowing the lowering of the possible opening of the stem loop structure of the molecular beacon". This phrase in considered indefinite because the claims do not define what constitutes the “possible opening”. Further it is also unclear as to how the probe itself can allow for lowering of its own stem loop structure, as opposed to, e.g., the inclusion of a modified nucleotide analog in the probe resulting in the lowering of the opening of the stem loop structure.

Claim 40 recites the limitation "the amplification enzyme mixture". There is insufficient antecedent basis for this limitation in the claim because the claims do not previously refer to an amplification mixture. Additionally it isn’t clear as to what is intended to be the relationship between the probe and the enzyme mixture, and therefore it is unclear how this phrase is intended to further limit the claims. In the

instant case the claims do not even state that the probe is present in an amplification mixture.

Claims 40, 45, 47, 49, and 51 are indefinite over the recitation of the phrase "having an affinity increasing modification is selected from the group consisting of…" in claim 40. This phrase should clarify that the probe stem comprises one or more nucleotides and the one or more nucleotides are selected from the group consisting of 2'-O-derivatized nucleotides, a locked nucleic acid, and a peptide nucleic acid.

Claims 41 and 43, 46, 48, 50, and 52 are indefinite over the recitation of the phrase "and/or" in claim 41. This phrase in considered indefinite because it is unclear if the probe stem has one or more unmodified nucleotides and then additional one or more unmodified nucleotides, i.e., are the unmodified nucleotides recited in lines 8 and 11 the same or different, and are the nucleotide analogs the same as or different from the 2'-O-methyl nucleotides.

Claims 41 and 43, 46, 48, 50, and 52 are indefinite over the recitation of the phrase "said probe allowing the lowering of the effect of sequence variations in a nucleic acid analyte". This phrase in considered indefinite because it is unclear how the probe changes the effect of sequence variations in the analyte. Further it is unclear what effect the sequence variations cause.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39-41 and 43-55 are rejected under 35 U.S.C. 102(e) as being anticipated by Becker (US Patent 2003/0105320 Filed 8/2002 with priority back to 8/2001) as evidenced by Majlessi (Nucleic Acids Research 1998).

Regarding Claim 39 Becker exemplifies a molecular beacon probe that was synthesized using 2'-o-methyl nucleotide analogs at all positions except for positions 5 and 21 which were occupied by deoxyribonucleotides (para 0196 and SEQ ID NO: 15). Thus Becker teaches a probe comprising one or more unmodified nucleotides and one or more nucleotide analogs having an affinity increasing modification (i.e. 2'-o-methyl nucleotides. As evidenced by Majlessi (Nucleic Acids Research 1998) the presence of 2'-o-methyl nucleotide analog in a probe will increase the melting temperature of that probe therefore it is an inherent property at a constant temperature of hybridization, the melting temperature of the probe with a target sequence in increased compared to the melting temperature of an unmodified probe with the same target sequence.

Regarding Claim 40 Becker exemplifies a molecular beacon probe wherein the probes stem comprises 2'-o-methyl nucleotide analogs at positions 1-4 and 22-25 and

deoxyribonucleotides at positions 5 and 21 (para 0196 and SEQ ID NO: 15). Thus Becker teaches a molecular beacon probe wherein the stem comprises one or more nucleotide analogs (i.e. 2'-o-derivatized nucleotide) and one or more unmodified nucleotides. Further it is an inherent property of this probe that the presence of the nucleotide analog allows for the lowering of the possible opening of the stem loop structure.

Regarding Claim 41 Becker exemplifies a molecular beacon probe wherein the probes stem comprises 2'-o-methyl nucleotide analogs at positions 1-4 and 22-25 and deoxyribonucleotides at positions 5 and 21 (para 0196 and SEQ ID NO: 15). Thus Becker teaches a molecular beacon probe wherein the stem comprises one or more nucleotide analogs (i.e. 2'-o-derivatized nucleotide) and one or more unmodified nucleotides. In view of the "and/or" language recited in the claim, the claim does not actually require a molecular beacon probe wherein the loop section comprises one or more nucleotide analogs with an affinity increasing modification and one or more unmodified nucleotides. However if the claims were amended to require molecular beacon probe wherein the loop section comprises one or more nucleotide analogs with an affinity increasing modification and one or more unmodified nucleotides, they would still be anticipated by Becker because Becker teaches pairs of molecular beacon probes wherein one of the probes in pair contains **at least one** modified nucleotide such as a 2'-o-methyl nucleotide analogs (para 0086). Becker further teaches that the probes in the pair can differ from one another in the loop region, the stem region, or in both their stem and loop regions (paras 0089, 0092). Further it is an inherent property of this

probe that the presence of the nucleotide analog allows for the lowering of the effect of sequence variations in a nucleic acid analyte and/or the possible opening of the stem loop structure.

Regarding Claims 43-44 Becker teaches a probe wherein the nucleotide analogs are 2'-o-derivatized nucleotides (para 0086-0087). Specifically the Becker teaches a probe wherein the 2'-o-derivatized nucleotide is a 2'-o-methyl nucleotide (para 0196).

Regarding Claims 45, 47, 49, and 51 Becker teaches pairs of molecular beacon probes wherein one of the probes in pair contains **at least one** modified nucleotide such as a 2'-o-methyl nucleotide analogs (para 0086). Becker further teaches that the probes in the pair can differ from one another in the loop region, the stem region, or in both their stem and loop regions (paras 0089, 0092). Thus this anticipates (i) molecular beacon probes wherein each base pair in the stem contains no more than one 2'-o-methyl nucleotide, (ii) molecular beacon probes wherein at least one base pair in the stem contains no nucleotide analogs having an affinity increasing modification, (iii) molecular beacon probes wherein one base pair in the stem contains no nucleotide analogs having an affinity increasing modification, and (iv) molecular beacon probes wherein each strand of the stem has at least one nucleotide analogs having an affinity increasing modification.

Regarding Claims 46, 48, 50, and 52 Becker teaches pairs of molecular beacon probes wherein one of the probes in pair contains **at least one** modified nucleotide such as a 2'-o-methyl nucleotide analogs (para 0086). Becker further teaches that the

probes in the pair can differ from one another in the loop region, the stem region, or in both their stem and loop regions (para 0089, 0092). Thus this anticipates (i) molecular beacon probes wherein each base pair in the stem contains no more than one 2'-o-methyl nucleotide, (ii) molecular beacon probes wherein at least one base pair in the stem contains no nucleotide analogs having an affinity increasing modification, (iii) molecular beacon probes wherein one base pair in the stem contains no nucleotide analogs having an affinity increasing modification, and (iv) molecular beacon probes wherein each strand of the stem has at least one nucleotide analogs having an affinity increasing modification.

Regarding Claims 53-55 Becker teaches kits comprising pairs of molecular beacon probes according to claims 39-41. Becker further teaches that the kits can comprise primers and polymerases (para 0139).

Conclusion

6. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634

/Carla Myers/
Primary Examiner, Art Unit 1634